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TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

ATTORNEY'S DOCKET NUMBER UTSC:772US

CONCERNING A SUBMISSION UNDER 35 U.S.C. 371 INTERNATIONAL FILING DATE INTERNATIONAL APPLICATION NO. PRIORITY DATE CLAIMED PCT/US2003/035139 November 4, 2003 November 4, 2002 TITLE OF INVENTION HA4, A NEW OSTEOBLAST-AND CHONDROCYTE-SPECIFIC SMALL SECRETED PEPTIDE, COMPOSITIONS AND METHODS OF USE APPLICANT(S) FOR DO/EO/US Benoit De Crombrugehe and Haruhiko Akiyama Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: This is a FIRST submission of items concerning a submission under 35 U.S.C. 371. This is a SECOND or SUBSEQUENT submission of items concerning a submission under 35 U.S.C. 371. This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below. The US has been elected (Article 31). A copy of the International Application as filed (35 U.S.C. 371(c)(2)) is attached hereto (required only if not communicated by the International Bureau). has been communicated by the International Bureau. is not required, as the application was filed in the United States Receiving Office (RO/US). An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). is attached hereto. has been previously submitted under 35 U.S.C. 154(d)(4). Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) are attached hereto (required only if not communicated by the International Bureau). have been communicated by the International Bureau. have not been made; however, the time limit for making such amendments has NOT expired. have not been made and will not be made. An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). An English language translation of the annexes of the International Preliminary Examination Report under PCT 10. Article 36 (35 U.S.C. 371(c)(5)). Items 11 to 20 below concern document(s) or information included: An Information Disclosure Statement under 37 CFR 1.97 and 1.98. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 12. **[** 13. L A preliminary amendment. An Application Data Sheet under 37 CFR 1.76. A substitute specification. A power of attorney and/or change of address letter. 17. V A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821- 1.825. 18. L A second copy of the published International Application under 35 U.S.C. 154(d)(4). A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). Other items or information: Statement as Required Under 37 CFR 1.821(f); CD-ROm; Paper Copy of Seq. Listing; Petition for Revival of an International Application Designating the United States Unintentionally Abandoned under 35 U.S.C. 371 and return postcard.

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450, DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. Page 1 of 2

JCOG Rec'd PCT/PTO 06 MAY 2005

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Approved for use through 3/31/2007. OMB 0651-0021

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. U.S. APPLICATION NO. TO KILD WILLS 39 FR 1.5) INTERNATIONAL APPLICATION NO. ATTORNEY'S DOCKET NUMBER PCT/US2003/035139 UTSC:772US CALCULATIONS PTO USE ONLY The following fees have been submitted Basic national fee.....\$300 Examination fee If International preliminary examination report prepared by USPTO and all claims satisfy provisions of \$ 23. Search fee Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority.....\$100 International Search Report prepared and provided to the Office......\$400 All other situations.....\$500 \$ TOTAL OF 21, 22 and 23 = Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof. RATE Extra Sheets Number of each additional 50 or fraction **Total Sheets** thereof (round up to a whole number) \$ Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest \$ claimed priority date (37 CFR 1.492(h)). NUMBER FILED RATE \$ **CLAIMS** NUMBER EXTRA \$ - 20 = x \$50 Total claims 59 \$200 \$ - 3 = x Independent claims 10 7 \$360 \$ MULTIPLE DEPENDENT CLAIM(S) (if applicable) + **TOTAL OF ABOVE CALCULATIONS =** \$ Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by 1/2. \$ Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest \$ claimed priority date (37 CFR 1.492(i)). **TOTAL NATIONAL FEE =** \$ Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property TOTAL FEES ENCLOSED = Amount to be \$ refunded: Amount to be \$ charged: A check in the amount of \$ to cover the above fees is enclosed. in the amount of \$ _____ to cover the above fees. Please charge my Deposit Account No. A duplicate copy of this sheet is enclosed. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit ___. A duplicate copy of this sheet is enclosed. Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038. NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status. SEND ALL CORRESPONDENCE TO: SIGNATURE. CUSTOMER NO. 32425 Steven L\ Highlander NAME EXPRESS MAIL NO: EV 603378518 US 37.642

REGISTRATION NUMBER

MAILING DATE: May 6, 2005